

## **REMARKS**

### **I. Preliminary remarks.**

Claims 88, 89, 97 and 100 are amended herein and new claims 101-109 are added. Support for the amendments to claims 88, 89, 97 and 100 can be found in the specification at pages 1, 4, 8, 9, 40, and 60-61. Support for new claims 101-109 can be found in the specification at pages 11, 15 and 38-40. Accordingly, no new matter has been added by the amendments made herein or the introduction of new claims 101-109.

### **II. The Rejection under 35 U.S.C. § 112, first paragraph, should be withdrawn.**

The Examiner maintained the rejection of claims 88, 89 and 91-96 as assertedly failing to be supported by an enabling specification. It is completely routine in the art to (1) make mutations or deletions in nucleotide sequences, (2) express nucleotide sequences in host cells, (3) test the expressed protein for activity, and (4) generate antibodies to proteins. The Examiner does not appear to dispute these general facts.

The enablement rejection appears to be based, in part, on the Examiner's assertion that the genus of polypeptides referenced in the claim includes polypeptides encoded by a non-coding strand of SEQ ID NOs: 1, 5, 9, 11, 13 or 15. Claims 88 and 89 have been amended to clarify that the polypeptides referenced are not encoded by a non-coding strand of SEQ ID NOs: 1, 5, 9, 11, 13 and 15.

The Examiner further rejected claims 88, 89 and 91-96 as assertedly not being enabled by the specification because the phrase "alter bone density" can be interpreted as either increasing or decreasing bone density. In response, claims 88, 89, 97 and 100 have been amended to recite "decrease bone mineral content." Support for this amendment is found throughout the specification in numerous statements that inhibitors of this protein increase bone mineral content, e.g. at page 1; page 8, lines 18-24; page 9, page 40, and pages 60-61. The specification discloses various routine assays well known in the art for assaying bone mineral content. See, page 63, lines 18-26. One of skill in the art could readily determine whether a protein decreases bone mineral content based on the teachings of the specification without undue experimentation.

The Examiner further asserts that the specification does not provide sufficient guidance for making mutants of TGF- $\beta$  protein (i.e., a polypeptide that decreases bone mineral content) that compete with the native TGF- $\beta$  protein. Such antagonist variants are not encompassed by the present claims. Claims 88, 89 and 91-96 are directed solely to *antibodies or antigen-binding fragments thereof* that specifically bind to a polypeptide that decreases bone mineral content.

For these reasons, undue experimentation is not required to make the claim-recited nucleic acid molecules and encoded polypeptides, and the claims are fully enabled.

**III. The rejection under 35 U.S.C. § 112, second paragraph, should be withdrawn.**

The Examiner rejected claim 88 under 35 U.S.C. § 112, second paragraph, as assertedly being indefinite for not reciting specific conditions of high stringency. In response, claim 88 has been amended to recite specific high stringency conditions. Support for this amendment can be found page 4, lines 16-19.

The Examiner also rejected claims 88 and 89 as assertedly being indefinite for reciting the phrase “alter bone density.” As discussed above in Section II, claims 88 and 89 have been amended to recite “decrease bone mineral content.”

In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 112, second paragraph, be withdrawn.

**IV. Obviousness-type double-patenting rejection.**

Claims 88, 89 and 91-100 were rejected under the judicially created doctrine of obviousness-type double patenting in view of claims 1-8 of U.S. Patent No. 6,804,453.

Applicants request that these double patenting rejection be held in abeyance until there is an indication of allowable subject matter. At that time, Applicants will consider filing appropriate disclaimer(s). It is premature to disclaim term before the scope of an allowable claim is clear.

**V. Conclusion**

In view of the above amendment, applicant believes the pending application is in condition for allowance. Please charge any deficiency in the fees to Deposit Account No. 13-2855.

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Respectfully submitted,

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